Citation:

Williams LJ, Rasmussen SA, Flores A, Kirby RS, Edmonds LD. Decline in the prevalence of spina bifida and anencephaly by race/ethnicity: 1995-2002. *Pediatrics.* 2005; 116: 580-586.

PubMed ID: 16140696

Study Design:

Trend study

Class:

D - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

The purpose of this paper is to characterize trends in the prevalence of spina bifida (SB) and anencephaly among Hispanic, non-Hispanic white, and non-Hispanic black births during the transition to mandatory folic acid fortification in the United States.

Inclusion Criteria:

Population-based birth defect surveillance systems were eligible to participate when they met the following criteria:

- The program's surveillance method identified cases from sources other than birth certificates
- Cases of anencephaly and spina bifida were reported by quarter of birth year from 1995 to 2002 (first quarter: January to March; second quarter: April to June; third quarter: July to September; fourth quarter: October to December)
- Cases and denominator data could be stratified into the following facial/ethnic categories: Hispanic, non-Hispanic white, and non-Hispanic black.

Exclusion Criteria:

Population-based birth defects surveillance systems were excluded for the following reasons:

- Unable to identify cases from sources other than birth certificates
- Unable to report cases of anencephaly and spina bifida by quarter of birth year from 1995 to 2002
- Data could not be stratified by race/ethnicity.

Description of Study Protocol:

Recruitment

- Data were collected from population-based birth defects surveillance systems meeting the inclusion criteria
- The following registries were included: Arkansas, California, Colorado, Delaware, Georgia, Hawaii,

Illinois, Iowa, Kentucky, Maryland, Missouri, New Jersey, New York, North Carolina, Oklahoma, Puerto Rico, South Carolina, Texas, Utah, West Virginia and Wisconsin. Nine of these surveillance systems also ascertained prenatally diagnosed cases as part of their surveillance program.

Design

- Data were collected regarding the prevalence of birth defects during the "pre-fortification period" (January 1995 to December 1996), "optional fortification period" (January 1997 to September 1998) and the "mandatory fortification period"(October 1998 to December 2002). These time periods reflect pregnancies that were exposed to various levels of folic acid fortification during the fourth week of gestation, the critical time of neural tube closure.
- Prevalence ratios were calculated to determine trends in birth defects during those time periods by race/ethnicity.

Statistical Analysis

- Prevalence ratios (PRs) were calculated by dividing the birth prevalence during the mandatory fortification period by the birth prevalence during the pre-fortification period
- The Taylor series method was used to calculate 95% CIs for the PRs
- Data were analyzed using the Statistical Analysis Battery for Epidemiologic Research.

Data Collection Summary:

- *Timing of measurements:* Data were collected at birth regarding the prevalence of either SB or anencephaly. Data were collected regarding the prevalence of birth defects during the "pre-fortification period" (January 1995 to December 1996), "optional fortification period" (January 1997 to September 1998), and the "mandatory fortification period" (October 1998 to December 2002).
- *Dependent variables:* Presence of either SB or anencephaly.
- *Independent variables:* Folic acid fortification.
- *Control variables:* Data were not collected on any other variables.

Description of Actual Data Sample:

- *Initial N:* From 1995 through 2002, the NTD Ascertainment Project covered:
  - 2.7 million Hispanic births
  - 6.7 million non-Hispanic white births
  - 1.7 million non-Hispanic black births
- *Attrition (final N):* 4,468 cases of SB and 2,625 cases of anencephaly
- *Age:* Prenatal terminations and live births
- *Ethnicity:* Hispanic, non-Hispanic white, non-Hispanic black_
- *Location:* Multi-state data from 21 states in the United States and Puerto Rico.

Summary of Results:

The study included data on 4,468 cases of SB and 2,625 cases of anencephaly. The prevalence of both defects was highest among Hispanic births, followed by non-Hispanic white births, with the lowest prevalence among non-Hispanic black births.

Table 1: Prevalence of Spina Bifida According to Race/Ethnicity Before and After Folic Acid Fortification

Race/Ethnic Category	Pre-fortification Period Prevalence*	Optional Fortification Period Prevalence	Mandatory Fortification Period Prevalence	Prevalence Ratio (Mandatory/Pre-fortification)	95% CI
Hispanic	6.49	5.52	4.1	0.64**	0.56-0.74
Non-Hispanic White	5.13	4.37	3.37	0.66**	0.60-0.72
Non-Hispanic Black	3.57	2.53	2.90	0.81	0.67-1.00

* Indicates prevalence per 10,000

** Indicates statistical significance.

Summary (Table 1)

The prevalence of SB significantly decreased 36% among Hispanic births and 34% among non-Hispanic white births; the magnitude of the decline among non-Hispanic black births was borderline statistically significant.

Table 2: Prevalence of Anencephaly According to Race/Ethnicity Before and After Folic Acid Fortification

Race/Ethnic Category	Pre-fortification Period Prevalence*	Optional Fortification Period Prevalence	Mandatory Fortification Period Prevalence	Prevalence Ratio (Mandatory/Pre-fortification)	95% CI
Hispanic	3.85	3.55	2.84	0.74**	0.62-0.88
Non-Hispanic White	2.79	2.12	1.98	0.71**	0.63-0.80
Non-Hispanic Black	1.98	1.82	1.80	0.91	0.70-1.19

** Indicates statistical significance.

Summary (Table 2)

Significant declines in anencephaly prevalence were observed among Hispanic and non-Hispanic white births; no significant decline was observed among non-Hispanic black births.

Author Conclusion:

- The results of this study suggest that folic acid fortification is associated with significant decreases in the prevalence of SB and anencephaly among non-Hispanic white and Hispanic births
- The magnitude of the reduction was similar between these two groups and was more pronounced for SB than for anencephaly
- The prevalence of NTDs among non-Hispanic black births did not decrease significantly.

Reviewer Comments:

Author mentioned that a combination of genetic and environmental factors are responsible for the differences in NTD risk observed among racial/ethnic groups.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	N/A
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	N/A
Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	No
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	???
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	???

3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	???
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	???
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	N/A
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	N/A
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	No
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	No
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	???

6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	N/A
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	No
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	No
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes

10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes